


Dematiaceous fungi

→  Topical imidazoles
Ciclopiroxamine
Thiabendazole

Fungi classified Based on pigmentation of Mycelial structure into:

- Fungi without pigment = hyaline
- Fungi e melanin in their cell wall ± Dematiaceous (Dark color)

• presentation:

① phaeo-hypho-mycosis:

- | | | | |
|---|---|----------------------------|--|
| <p><u>Superficial</u></p> <ul style="list-style-type: none"> - organism in outer layer of Hair-Skin-Nail - minimal Host Response • Tinea-nigra • Black-piedra | <p><u>Cutaneous</u></p> <ul style="list-style-type: none"> - organism in Epidermis - Dermis → elicit inflammatory Host reaction → invade by skin or Nail • Hendersonula • Toruloides • Scytalidium Hyalinum • Alternaria species | <p><u>Subcutaneous</u></p> | <p><u>Systemic</u></p> <ul style="list-style-type: none"> • Cerebral Cladosporiasis |
|---|---|----------------------------|--|

③ chromo-Blasto-mycosis

∴ Tinea.Nigra ∴

→ D.F: its one of superficial phaeohyphomycoses
Caused By: Black yeast {phaeo-annellomyces werneckii}

→ Diagnosis:

- Direct KOH examination: Scales → Dark pigmented septate hyphae or Budding

• Culture: Sabouraud's glucose agar
→ 2 phases → Early: pigmented yeast phase
→ Late: hyphal mold phase

microscopically: septate dark hyphae bearing annellides

• Histopathology: Hyphae present in Strat. Corneum / e minimal inflammatory Reaction in the Dermis

• Clinically: Sharply defined - Asymptomatic - nonScaly - Brown Black macules - palm - soles

Piedra

Trinea Nodosa
Trichosporosis

- Df: it's a Fungus infection Confined to :-
Hair shaft of scalp, Beard, Moustache
• With the formation of Superficial Nodules
(Piedra = stone)

• DD: Hair shaft abnormalities

- Treatment :-
1- Cutting of the infected Hair
2- Benzoic acid Compound
3- Oral **terbinafine**
4- Oral **itraconazole** 100 mg
Daily → until Culture -ve
(in white Piedra)

	<u>Black Piedra</u>	<u>White Piedra</u>
Fungus	→ <i>Piedraia Hortae</i> → <u>related to</u> superficial phaeo-hypho-mycosis	- <i>Trichosporon beigellii</i> - <u>Some cases</u> : Sexually transmitted, ↑ Carriage Rate of <i>T. beigellii</i> in perianal Region in HIV +ve
Clinical	→ Asymptomatic gritty • Hard Black multiple firmly adherent <u>Nodules</u> on Hair shaft (mainly scalp)	• White - tan - soft Nodules along Hair shaft. That can be easily → pulled from the Hair (mainly Beard mustache - pubic) • Invasive opportunistic infection may occur in → Immunosuppressed phn
Diagnosis	① <u>Direct KOH</u> • Densely packed Rhomboid cells + Branching pigmented Hyphae • <u>Asci</u> : contain 2-8 ascospores (This is the <u>only</u> Fungal in which Sexual spores are found in the <u>parasitic phase</u>) ② <u>Culture on Sabouraud's agar</u> • Small Dark colonies - elevated at center ③ <u>Microscopic</u> : • Septate Dark hyphae & intercalary swollen chlamydospore-like [37]	• <u>mixture of</u> : Yeast - hyphae - pseudohyphae arthrospores • Creamy wrinkled colonies → later → deeply furrowed "Cycloheximide → inhibit its growth" • Septate hyphae that → fragment into arthroconidia. • Blastoconidia - pseudohyphae → may present

Tinea-like infections by the Saprophytic Moulds:

The 2 moulds

→ Both Cause Similar tinea-like inf in Hand, Feet, Nail

[1] Tinea pedis :-

- Dry-moccasin type associated w/ T. rubrum with similar unilateral lesion in palm
- Interdigital Type
- Vesiculobulbous Type: Commonly T. mentagrophytes was Not recorded

[2] Onychomycosis : DLSO - PWSO - TDO

- start: at lateral and distal edges of the nail extensive undermining of the nail without thickening of nail plate
- Paronychia: often accompanies these changes
- Diagnosis :-

- 1- Direct KOH :- non-pigmented hyphae - more irregular than Dermatophytes
- 2- Culture : show H. toruloides : light color cottony colony → e age Darkens.

• III : Topical e Imidazole or Whitfield #

[38]

• Scytalidium dimidiatum

- Dermataceous mould

- Gray - Black color

• Scytalidium hyalinum

- albino form of S. dimidiatum

Other Saprophytic moulds

→ Commonly present small amount, Contaminants of normal skin (Scalp - toe clefts)

Infection of skin By Alternaria species

- nodular-ulcerative Dermal infection
- e 2ry Epidermal involvement
- Localized infection over → exposed part (Dorsa of Hands)
- in AIDS → widespread Dermal lesion
- Diagnosis :

- Culture
- Histopathology: pigmented Hyphae in Epidermis non-pigmented in Dermis

• HI : Itraconazole
Fluconazole

Onychomycosis

- 2ry invaders to already Damaged nail plate By Trauma, Ischemia

• Scopulariopsis brevicaulis

- Doesn't attack the skin
- Cause nail Dystrophy in Big toe e Cinnamon color in Subungual Hyperkeratosis
- HI : 40% Urea paste then Remove nail plate, AZole in nail Bed

• Aspergillus species

- live in outer or dorsal area of nail plate

① Topical Antifungals ↗ Topical ↘ systemic

II with mainly Antidermatophyte Action

- ① Whitfield Ointment → Salicylic acid 3: Keratolytic
S/E: Irritation systemic absorption → Salicylism
→ Benzoic acid 6: fungistatic
- ② Undecylenic acid and its salt powder
- ③ Tolnaftate 1% ointment: "TineaCure" "Tineadem"
Fungicidal action by inhibition of Squalene epoxidase
- ④ Castellani's Paint:
= magenta Red - Boric acid - phenol - Alcohol
- Resorcinol - acetone - aqua
- eliminating the Fuchsin → makes it colorless & out
loss of activity - has antibacterial action
- used in intertriginous area: interdigital tinea pedis
- S/E: Staining - irritation - Toxic phenol reaction

III with mainly Anticandidal action:

- ① Gentian Violet: 1% in aqueous or alcohol
- S/E: staining - skin irritation
- ② Nystatin:
- ③ K permanganate: 1/5000 solution
nonspecific antifungal activity

III with mainly Anti-pityriasis & Versicolor action:

- ① Selenium sulfide 2.5%
 - ② Zinc Pyrithione
 - ③ Sodium thiosulphate 20%
- used also in Seb. Dermatitis

IV e Broad spectrum activity:

- ① Ciclopiroxolamine Cream (Batrafen)
• act by inhibition of synthesis of cell membrane protein → antibacterial • anti-inflammatory activity
• Ciclopirox 8% → able to penetrate Nail, once daily
→ effective in t/t of onychomycosis
- ② Haloprogin 1% (Halotex)
- ③ Iodo-chlor-hydroxy-quin: (Vioform)
- antibacterial - mild antifungal - S/E: Neurotoxicity
- ④ Propylthiopylone glycol: Keratolytic - antimycotic
propylene glycol - urea - lactic acid → in onychomycosis
- ⑤ Imidazoles miconazole - iso-tio - seita - clotri - keto
- ⑥ Allylamines: Terbinafine 1% "Lamisil" - Naftifine 1%
- ⑦ Amorolfine 0.25% inhibit ergosterol synthesis

② Systemic :-

according to site of action :-

- at the nuclear level
- at Cytoplasmic membrane level
 - polyenes : Nystatin, Amph-B
 - Azoles : Keto-itra-flu
 - Allylamines : Terbinafine
- at level of cell wall : Echinocandins
- on mitotic spindle : Griseofulvin

① Griseofulvin

- metabolic product of *Penicillium griseofulvum*

- Pharmacokinetics :

- ① weak water soluble
 - ② poorly absorbed in GIT
 - ③ Absorption enhanced by microcrystalline and fatty acid diet
 - ④ metabolized in Liver
 - ⑤ Rapidly delivered to st. Corneum in 4-8 hrs
- Through : • Direct Diffusion
• Sweating • evaporation of fluid from cut. surface → accumulation of drug in st. Corneum
- ⑥ Drug Rapidly eliminated : from skin 48-72 hr from discontinuation of drug
- ⑦ mode of action : ① inhibit nucleic acid synthesis
② inhibit microtubule function

- Indication + Dosage :

- Fungistatic • effective in Dermatophytes infection only • Not effective in Candida & PV

Dose : Tab = 125 mg (12.5 mg/kg)

2-4 weeks → Tinea Cruris - Corporis

6-8 weeks → Tinea Capitis

4-9 months → Tinea-unguium of fingernail

6-12 months → Toe nail

(40)

② Ketoconazole (Nizoral)

- it's the first oral Broad spectrum antifungal

- 1- well absorbed after : Oral administration
 - 2- Gastric acidity : essential (taken after meal)
 - 3- Antacids - H₂ Receptor Blockers : (Cimetidine - ranitidine) should Avoided X
 - 4- metabolized in Liver
 - 5- Rapidly delivered to st. Corneum : - within 3 hrs
- Through : • Sweat • Sebum • incorporation into the epidermal Basal cells
- 6- mode of action : similar to Azoles, Disrupts Ergosterol biosynthesis By inhibit Cytochrome P-450 enzyme Lanosterol 14- Demethylase.

Tab = 200 mg

① Severe superficial Dermatophytosis 200 mg/day

T. Cruris - Corporis - Capitis → 2-8 wks

Onychomycosis → 4-6 months Fingernail • 8-18 toenail

② PV : 200 mg/d for 5-10 Days

③ Candidiasis : VVC (400 mg x 5 days), CMC, Onych

④ other : SD - pityrosporum folliculitis • Cut. leishmaniasis
Cushing Disease - Cancer prostate (as steroid inhibitor)

Griseofulvin

Side effect:

- ① GIT: Nausea - Vomiting - heart Burn
- ② Headache ③ Cut. Drug eruption photosensitivity
urticaria - Lichen planus - exacerbation of
Lupus Erythematus
- ④ taking Drug & meal → Reduce symptoms

Contraindications: pregnancy porphyria, hepatic failure

Drug Interaction:

- ① phenobarbitone ↓ griseofulvin absorption from gut
- ② Griseofulvin
→ Reduce the anticoagulant effect of warfarin
→ Reduce Cyclosporine level
→ Reduce the effectiveness of OCPs

Causes of griseofulvin failure:

- ① Failure of absorption
- ② ↓ peripheral circulation
- ③ Co-existing pathology
- ④ 2ry infection
- ⑤ Idiopathic Resistance

41

Ketoconazole

- 1-inhibit fungal Cytochrome P-450 enzyme
- 2-interfere w mammalian Cyt. P-450 enzyme system in adrenal - testis - ovary - liver
- 3-GIT: vomiting - Nausea 4- Pruritis 5- Rash
- 6- Hepatotoxicity
- 7- Inhibition of Steroidogenesis (antiandrogen effect)
↓ libido - impotence - gynaecomastia - menstrual irregularity

Pregnancy - lactation

Ketoconazole

- ↑↑ plasma level of cyclosporine
- potentiate suppression of adrenal gland caused by Steroid
- potentiate the anticoagulant effect of Warfarin
- Reduce the effect of OCPs
- Rifampin - Isoniazid → ↓↓ Ketoconazole level

→ Hypo - achlorhydria → Common in HIV →
Drug Ketoconazole → Require acidic medium for
Their absorption → Should given w acidic fruit juice
→ No longer prescribe Ketoconazole as 1st Drug therapy
for any fungal infection Due to Risk of severe liver injury
and adrenal insufficiency

③ FluCytosine

• mode of action:

- converted to 5-Fluorouracil
→ which interfere w/ Fungal
nucleic acid synthesis

→ Usually Combined w/

Amphotericin B in Ht of
Cryptococcal meningitis
Candidiasis - Aspergilluses
Chromomycosis

Dose: 50-150 mg/kg/day
every 6 hrs
For 6-12 weeks

side effect:

- ① Bone marrow depression
- ② Hepatic Dysfunction
- ③ Enterocolitis

④ potassium iodide

- By mediated through the
antifungal properties of Molecular
iodine

- Saturated solution of potassium
iodide (SSKI) 10m/mL
given starting with 3ml (10drops)
3 times Daily → up to 15 ml
3 times Daily
For 6-8 wks

- Nausea - vomiting - parotid
swelling - acneform eruption -
- Dermatitis herpetiformis

X Contraind: pregnancy - DH

SSKI → should Diluted in water
or Juice to minimize Bitter taste
- Crystallization → may occur @ Cold
Temperature → Rewarming + shaking

⑤ pol yenes

- They Bind with the Cell membrane
Ergosterols → Result in:
altered Cellular permeability e⁻
leakage of Cellular Contents →
Cell Death
- They Bind also (But lesser extent)
to cholesterol in mammalian cells

- 0.4 - 0.6 mg/kg/day
- For 6-12 week
- By slow single IV infusion
- 0.25 mg/kg/day → Diluted
with 5% glucose.

- Fever - Nausea - Vomiting
- Bone marrow Toxicity
- Nephrotoxicity
- Hypokalemia

⑥ Triazoles • Itraconazole

- Keratophilic • lipophilic Broad spectrum, Oral

- pharmacokinetics:

- Water soluble • Rapidly absorbed after oral
- Gastric acidity is essential → should taken shortly after meal • Avoid → Antacids
- metabolized in Liver • Delivered to skin through

- ① sweat within 24 hr
 - ② Sebum → major Route
 - ③ incorporation into the epidermal Basal cells occur at slow rate → help maintain Drug level at skin for 3-4 weeks after Discontinue Drug
- High affinity to: adipose tissue, skin, Nail, vagina

- Indication- Dosage: Cap = 100 mg

- ① T. capitis: 5 mg/kg/d → For 4-6 weeks
pulse therapy → 5 mg/kg/d → 1 week
Then 2 wks off → followed by 1 wk with Drug
- ② T. Cruris/Corporis: 100 mg/once/daily → 15 Days
or 200 mg/daily → 7 days
- ③ T. pedis/manuum: 100 mg/once/daily → 30 days
or 400 mg/daily → 7 days
- ④ PV: 200 mg/daily → 7 days
- ⑤ Onychomycosis: pulse therapy = 200 mg/twice
Daily → 7 days of each month for 3-4 months

• Fluconazole

- Broad spectrum - available in Oral, parenteral form

- Differ from other AZoles in:

- 1) Low molecular weight
- 2) Higher water solubility
- 3) Gastric acidity → Not essential for its absorption
- 4) the majority of Drug → Circulate in its free form
- 5) excellent penetration into CSF
- 6) it Doesn't undergo significant First Pass metabolism

- Cap = 150 mg
- ① T. Capitis: 6 mg/kg/d → 20 Days
 - ② T. Cruris-Corporis-pedis ^{Candidiasis} ~~Cut leishmaniasis~~
one Cap/week → for 3-4 weeks
 - ③ Onychomycosis: one Cap/week → 6-9 months
 - ④ PV: 2 Cap → may repeated after 2 weeks
 - ⑤ Candidiasis:
VVC → Single Dose → Cap = 150 mg
CMC → 50 mg/daily → 10 Days
 - ⑥ Systemic fungus infection:
Cryptococcal meningitis

Itraconazole

⑥ Candidiasis:

VVC → 200 mg - twice daily → For one day

Oral → 100 mg or 200 mg daily / For 15 Days

CMC → 100 mg daily → For 3-12 week

⑦ Systemic Fungal inf: sporotrichosis - Aspergilliosis For Long periods

- side effects: minimal: N + V - Rash

- Contraindications: Pregnancy

- Drug interaction:

• Drugs ↓↓ Serum level of Itraconazole:

Rifampin - Isoniazid - anticonvulsants (phenytoin)

• Itraconazole potentiate the effect of some Drugs

- Through inhibition of cytochrome P3A4 of serum level of Drug → which Require → Hepatic metabolism By CYP3A4 enzyme to Be Removed

- Antihistamines (Terfenadine)

- Benzodiazepines (Triazolam - midazolam)

- Buspirone - Busulfan - CCB - Cisapride

- Cyclosporine - Lovastatin - Simvastatin

- Phenytoin - Oral hypoglycemics - Sildenafil

- Tacrolimus - warafin

• Co-administrate Itraconazole & HIV protease inhibitor

- lead to change in plasma Concentration of Both Drugs

Fluconazole

Few - N + V - Headache - Erythema multiforme

• Rifampin → ↓↓ Fluconazole level

• Fluconazole → ↑↑ plasma level of some Drugs:

→ Antihistamines (Terfenadine - Astemizole)

→ Benzodiazepines

→ Cisapride - Cyclosporine

→ Oral Hypoglycemic agents → phenytoin

→ Tacrolimus - warafin

⑦ Allylamines:

- 2 generations:
 - Naftifine → Topical
 - Terbinafine → Topical + systemic

- Pharmacokinetics:

1. After Oral intake → terbinafine is well absorbed
2. gastric acidity is Not essential
3. High lipophilic - KeraFophilic → accumulation in adipose tissue and skin
4. Rapidly Delivered to St. Corneum - Nail ~
5. elimination from skin is Biphaseic.

- Mechanism of Action:

- ① Disrupts - ergosterol biosynthesis → at Early stage
(By) inhibition of Squalene epoxidase @ Fungal growth arrest (fungistatic) → Squalene accumulates with the fungal cell with Death (fungicidal)
- ② Has minimal effect on mammalian cholesterol synthesis
- ③ Has No effect on cytochrome P450 → So No effect on cortisol or testosterone levels
- ④ inhibition of CYP 2D6 By Terbinafine

- Indications + Dosage:

- mainly → against Dermatophytes
- less effective → against Candida
- No effect on → PV

(Terbinafine) → Lamisil = one Tab = 250mg/day

- T. Capitis = 3-6 mg/kg → 4 weeks
- M. Canis → 8 weeks
- T. Cruris - Corporis → 2 weeks / one week is effective
- T. Pedis → 2 weeks
- onychomycosis → For 6 weeks in finger nails - 12 wks → toe nail

- Side effects:

- Dyspnea - N+V - Rash
- Terbinafine → induces SLE with High titres of ANAs + antihistone Abs

- Drug interactions:

By action on CYP 2D6 - or 1A2

- Cimetidine : ↑ Terbinafine level
- Rifampicin : ↓ Terbinafine level
- Terbinafine : ↓ Cyclosporine level

⑧ Echinocandins:

• Caspofungin - Micafungin - Cilafungin
Anidulafungin

- effective against: Candida and Aspergillus

- mode of action: inhibit the synthesis of
B-(1,3) D-glucan → an essential fungal
cell wall component

↓
Alteration in fungal cell wall permeability

- Anti-inflammatory effects of Antifungal agents:

① Allylamines - Benzylamine →
have great anti-inflammatory action than
Azole antifungals

② Naftifine → inhibit chemotaxis and
the production of reactive oxygen
intermediates by neutrophils

③ Azoles: inhibit
Neutrophil chemotaxis
↓
Calmodulin activity
↓
synthesis of leukotrienes
↓
PG-Histamine Release
from mast cells

④ Ketoconazole: has anti-inflammatory activity
comparable to that of hydrocortisone

⑤ Ciclopiroxolamine: inhibit PG and
leukotrienes synthesis

Deep Mycoses @ S.C :-

* Classification:

↳ D Sub Cutaneous mycoses

- Sporotrichosis
- Chromoblastomycosis
- Mycetoma
- Phaeohyphomycosis

↳ II) Systemic or Pulmonary:

- Blastomycosis
- Coccidioidomycosis
- Histoplasmosis
- Para-Coccidioidomycosis

↳ II) Opportunistic Mycoses

- Cryptomycosis
- Mucormycosis
- Aspergillosis
- Fusarium

1- * Sporotrichosis *

- D.F → Chronic lymphatic S.C. fungal infection
- Etiology → *Sporothrix Schenckii* (Dimorphic aerobic fungus)
 - ↳ Found in: Soil
 - ↳ introduced into Skin By Trauma and Direct inoculation
- Epidemiology →

occur in tropics - South - Central America - Egypt

mine workers
florists
gardeners

• Clinical →

Cutaneous forms

1) Lympho Cutaneous variety

- The commonest
- it follows the implantation of spores in wound
- Sporotrichotic **Chancre**
- occur in exposed skin: limbs
- as: Nodule - Pustule → Break Down → ulcer
- Involvement of: lymphatics → chain of lymphatic Nodules → Soften → ulcerate
- Regional L-N: rarely → Become Swollen → Break Down
- heals: spontaneously → leaving → the lymph nodes Enlarged

II) Endemic "fixed" variety:

pathogen → Remain Localized at the point of inoculation → Pimple form, Nodular
Ulcerated → extensive verrucous, infiltrated plaques

Extracutaneous forms

- follow inhalation → in phn & defect in host defense
- e.g. alcoholics - AIDS
- ulcerated Nodules on the skin and M.M. Visceral lesion

2- *Chromoblastomycosis*

• Diagnosis:

Direct KOH: No value → as the organisms are few in numbers

II) Fluorescent antibody techniques:

III) Culture: "on Sabouraud agar"

→ at Room temperature
→ Compact moist white with wrinkled surface

→ Later aerial mycelium is formed and colonies → Become darker.

→ Microscopically → narrow hyphae with small oval - Triangular Conidia

IV) Histology:

- Mixed granulomatous Reaction & Neutrophil microabscess

- Present as: Small - Cigar shaped or oval yeasts → Surrounded by Thick Radiating eosinophilic fringe Forming → **Asteroid Bodies**

• Treatment:

→ Spontaneous Remission
→ K iodide (SSKI) → 5 drops initially
→ ↑ to 50 Drops 3 times a day → Continued for 3-4 weeks after Cure

→ Itraconazole: 100-200 mg daily (48)
→ Amphotericin B, Miconazole IV

• Etiology: Several Dematiaceous Fungi

• *Phialophora verrucosa* • *Fonsecaea pedrosoi*
• *F. Compactum* • *Wangiella dermatitidis*

→ Isolated From: Wood - Soil → Acquired inf: Trauma Inoculation

• Clinical: in

→ Exposed sites: Feet - legs
as: Painless - slow-growing warty papules → Enlarge to form → Large Brownish warty plaque

→ Some lesions → Ulcerated on the surface

→ 2ry infections → Lymphatic Stasis with the production of → **Elephantiasis**

• Diagnosis:

Direct KOH: Deeply pigmented thick wall Bodies "Medlar Bodies" Uniform, sclerotic Bodies

→ The organism is Not → Yeast, Not multiply By Budding
→ Multiply By Splitting → Formation of Cross walls within mature Cells

II) Culture: Slowly growing - Dark velvety colonies

III) Histopathology: F.B granuloma, Epidermal Hyperplasia - pseudoeplitheliomatous growth, some abscess formation

• Itl ① Itraconazole → 200mg/d. e or e out Fluocytosine

② Fluocytosine → 100-200 mg/d - e or e out Amphotericin B

③ Surgical Removal in very small. Early lesions

3. * Phaeoerythromycosis *

(Cystic Chromomycosis)

• D.F.: rare localized S.C cyst Caused By many Dematiaceous fungi

- *Exophiala jeanselmei*
- Acquired infection: Trauma, implantation

• Lesion:

- Large Cyst → Containing Black hyphae or Yeast & thickened overlying Epidermis
- Lymphatic spread → Rare.

• Treatment:

- ① Surgical excision
- ② Itraconazole

• Etiology: Just → Eumycetoma
→ Actinomycetoma

→ The organism occur as → Saprophytes in the Soil → from which infection of S.C tissue of the skin occur through: penetrating injury

→ The organism Survive in SC tissue → Because they are able to Develop → ① thick wall
② extracellular melanin Deposition
→ which allow them to Resist Neutrophil attack

• Clinical:

→ Occurs in Foot or Lower leg "site of Trauma"
→ Slowly progressive → firm painless Nodules
"Irregular Lumpy appearance" → which Break Down → Discharge Pus → Containing grains of different colors through → Multiple sinus Tracts
→ Extension to → underlying Bones, Joints
→ periostritis, osteomyelitis, arthritis

4. * Mycetoma *

("Madura Foot")

• D.F.: - tumor produced By fungi

• ch. ch. By:

- ① Localized Swelling & Severe affection of S.C tissue, Bone, feet, Hands
- ② Formation of Draining Sinuses,
- ③ granules of different colors → are Discharged

Etiology: There are 2 main groups, with the same clinical picture:

Type of mycetoma	Causative organism	Color of grains
Eumycetoma "fungi" IP: 20 yrs	<ul style="list-style-type: none"> • <i>Madurella mycetomatis</i> • <i>M. grisea</i> • <i>Leptosphaeria senegalensis</i> • <i>Pseudallescheria boydii</i> • <i>Acremonium spp</i> • <i>Fusarium spp</i> → 	<ul style="list-style-type: none"> • Black • White • Yellow
Acetinomycetoma "actinomycetes" IP: 5 yrs	<ul style="list-style-type: none"> • <i>Nocardia brasiliensis</i> • <i>N. asteroides</i> • <i>Streptomyces somaliensis</i> • <i>Actinomadura madurae</i> • <i>A. Pelletierii</i> → 	<ul style="list-style-type: none"> • White or not present • Yellow • Red

• Diagnosis:

① Direct KOH of pus: color of granules → Determine their fungal or actinomycete nature

② Culture on Sabouraud's agars:

Fungi

(Chloramphenicol only)
at Room temp →
growth occur in
5-10 Days

Actinomycetes

(Cycloheximide only)
- at Room temp
- growth occur →
2-3 Days

③ Histology:

Chronic granulomatous Reaction
e abscess formation -
Containing → ch-ch granules +
Dense fibrosis

• treatment:

I excision → of Localized lesion

II Actinomycetoma → Dapsone
with Streptomycin, Sulphamethoxazole

Trimethoprim + Streptomycin, Rifampin

III Eumycetoma → Ketoconazole
Itraconazole, [50]

② Systemic:

1 * Blastomycosis "North American"

• Etiology: Blastomycetes Dermatitis

• Clinical:

Try pulmonary

- similar to pulmonary T.B
- May Be Asymptomatic
- or: Low Grade Fever
- Cough-Hemoptysis -
- rate → Erythema Nodosum
- Disseminated lesions
- Skin → Symmetrical
- Papular - Nodules →
- ulcerate → Discharge pus
- Enlargement of lesion → Serpiginous warty Borders and
- Central scarring.

Try Cutaneous

- V. Rare
- follow: Trauma to skin.
- Inoculation of Fungus
- Erythematous in directed area e Chancre → appear
- after 1-2 weeks e
- lymphangitis-lymphadenopathy

• Diagnosis

① KOH examination: Thick wall - Rounded - Refractile spherical
Cells e Broad Based Buds

② Culture: at Room temp (Mycelial form) → small oval conidia
at 37°C (Yeast form) → with ch-ch Buds

③ Histopathology: - Epidermal Hyperplasia - inflammatory
infiltrate e Small abscess - Langhan's giant cells

• treatment: 1) Amphotericin B 2) Ketoconazole 3) Itraconazole

2- * Coccidioidomycosis *

• Etiology: *C. immitis*

• Clinical:

↳ Iry pulmonary

- Similar to T.B
- Asymptomatic
- or pyrexia - cough
- Short Erythematous Rash
- Disseminated lesions
- mainly in: Negroid or immunosuppressed as AIDs

- in skin: (abscess - granuloma - ulcer - sinuses)

• Diagnosis:

↳ KOH of sputum - CSF: Large globular spherules (sporangia)

↳ Culture Colonies: Mycelial - white - cottony

↳ Microscopy: Arthrospores - produced at intervals along the length of Hyphae

↳ Histopathology: in the dermis as spherules with endospores Better: PAS stain

↳ Serological test: precipitant - CF antibodies

↳ Skin test: \bar{C} Coccidioidin \rightarrow little value

↳ Iry Cutaneous

- firm painless indurated nodules 1-3 weeks after some form of Local trauma
- \bar{c} Regional lymphadenopathy

• treatment: 1) Amphotericin B 2) Ketoconazole

3- * Histoplasmosis "Darling's disease"

• Etiology: *Histoplasma Capsulatum*.

unique Fungus: intracellular, parasitizing the Reticuloendothelial system - involve: spleen - liver

• Clinical:

① Asymptomatic: with +ve skin test \bar{c} Histoplasmin

② pulmonary: Acute \bar{c} fever - chest pain - cough - weight loss, \bar{c} Erythema multiforme or E. Nodosum
X-ray: Diffuse mottling or localized infiltration
Chronic: - occurring in Adults \rightarrow simulating pulmonary T.B

③ Disseminated Form: Acute (fatal) \bar{c} prominent pulmonary signs - Splenomegaly - lymphadenopathy - fever - mucocutaneous granulomas

- seen in AIDs \bar{c} more skin affection \leftarrow papules small nodules
chronic: \bar{c} Manifest. of Addison's Disease

D.t adrenal infiltration + large chronic mouth ulcer

④ Iry Cutaneous Form:

v. rare - occurring after inoculation of the organism into the skin \bar{c} Nodule or indurated ulcer associated \bar{c} Local lymphadenopathy

(5)

• Diagnosis:

- By: Identifying small intracellular yeast-like cells of Histoplasma in Culture. Histopathology - Blood smear
- Direct KOH of Sputum: -ve Results as the yeast is intracellular and Destroyed By KOH

- Culture: grow as a mould
white cottony colonies & large Rounded Tuberculate Macroconidia
- The smaller microconidia are infectious
- Cautions → as the fungus is highly infectious

• Biopsy:

The budding yeasts are found inside histiocytes

- Histoplasmin Skin test: No Value

- Serological tests: i) Rising CF titre indicate Dissemination ii) precipitins: H - M antigens
Correlate → well & active infection
- iii) Detection of circulation Histoplasma antigens

- Treatment: i) Itraconazole ii) oral Ketoconazole
iii) Amphotericin B.

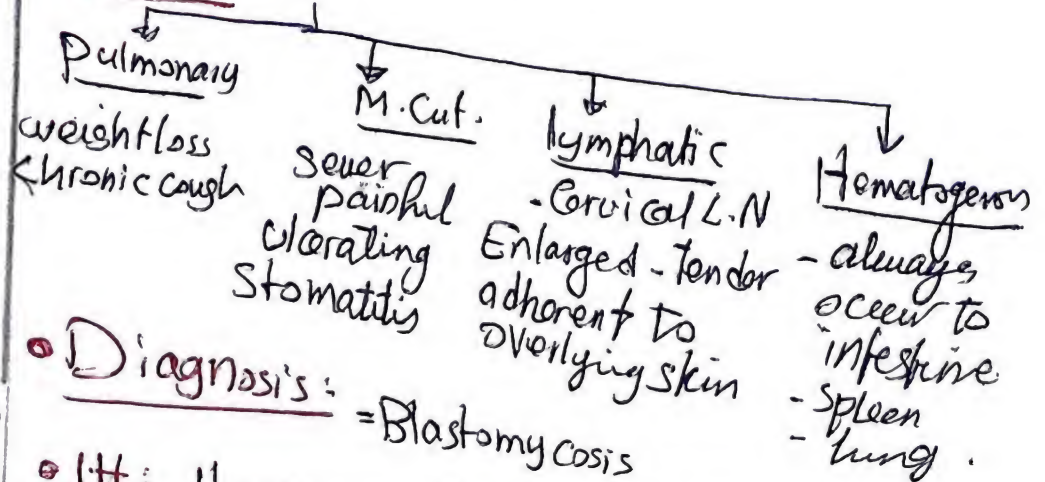
• African Histoplasmosis:

Commonly affect Bone or Skin →
Producing Molluscum Contagiosum-like papules,
abscess, or ulcers

4-★ Para-Coccidioidomycosis (South American)

- Etiology: P. brasiliensis

• Clinical:



- Diagnosis: = Blastomycosis

- Itt: Itraconazole (Drug of choice)
- Ketoconazole
- Amphotericin B

5 ★ Penicilliosis ★

- Etiology *penicillium marneffei* show → Unusual pattern of Dimorphism
 - It develop - Yeast like cells → that reproduce
 - Septal formation → Dividing the cell into two.

• Clinical:




- ① Localized pulmonary: as chronic
- ② Disseminated lesions: in many organs: liver - GIT - spleen
- ③ Skin lesions: (50% of pts)
 - Umbilicated papules on Face, trunk
 - may Enlarge - ulcerate

• Diagnosis:

- ① Culture: *P. marneffei* → green or grayish mould → that produce typical conidiospores → Diffusible Red pigment
- ② Histopathology (stain e⁻ methanine silver)
 - Small oval cells
 - Large Banana shaped cells

• treatment:

- ① Amphotericin B
- ② Itraconazole

	Blastomycosis (North American blastomycosis)	Coccidioido- mycosis	Histoplasmosis	Paracoccidioidomycosis (South American blastomycosis)
Etiology and mode of infection	<i>B. dermatitidis</i>	<i>C. immitis</i>	<i>H. capsulatum</i>	<i>P. brasiliensis</i>
	– mainly by inhalation of spores from saprophytic source –			
Epidemiology	North America & Asia. Adult males (30-50 yrs).	South western states of USA. – All ages & both sexes –	Tropical areas of Americas.	Latin America. Adult males (30-50 yrs).
Clinically				
• 1ry pulmonary (as pul. TB)	May be asymptomatic or there is fever, cough, chest pain & rarely erythema nodosum.			
• Dissemination	May occur in many organs as spleen, liver, bone & skin (ulcers, sinuses, etc...)			
• 1ry cutaneous (rare)	Follows trauma & inoculation of organism → indurated nodules + LN++.			Differs from blasto- mycosis by gum affec- tion with loss of teeth + marked LN++.
Diagnosis				
• KOH ex. of sputum	Thick, refractile walled cells with broad based buds. 	Large globular, spherules, with en- dospores. 	–ve	Rounded, refractile cells with multiple budding. 
• Biopsy			Intracellular budding yeasts.	
• Culture	Mycelial white & cottony colonies producing small rounded conidia.	Mycelial white & cottony colonies producing arthro- spores along the length of hyphae.	White, cottony colonies with characteristic large rounded tuberculate macroconidia.	Slower growing & fewer spores than <i>B.</i> <i>dermatitidis</i> .
	CAUTION? Fungus is highly infectious!!			
• Serological tests	– Of diagnostic value –			
Treatment	– Itraconazole or ketoconazole –			

III) Opportunistic mycoses

HL

These mycoses develop only in hosts with local or systemic impairment of their defenses.

Cryptococcosis

Etiology: *Cryptococcus neoformans*. It exists as a saprophytic yeast mainly in the soils enriched by pigeon excreta due to the presence of creatinine. Under certain conditions a sexual stage "*Filobasidiella neoformans*" is formed which, unlike all pathogenic fungi, is a basidiomycete. Infection is acquired mainly by **inhalation** affecting primarily the respiratory tract. There is a marked predilection for the brain and meninges, although skin and other organs could be affected.

Opportunistic mycoses

- Cryptococcosis
- Mucormycosis
- Aspergillosis
- Fusariosis
- Candidiasis

Epidemiology: It occurs worldwide, more between 30-50 yrs old.

Predisposing factors: Impairment in CMI due to (1) lymphomas, (2) carcinomas, (3) treatment with systemic steroids or cytotoxic drugs, or (4) AIDS which is the main underlying disease, where cryptococcosis occur in 3-12% of AIDS patients mainly in the form of meningitis.

Clinical features

- **Pulmonary disease:** There is fever, cough, dyspnea, weight loss and chest pain. Chest X-ray reveals bilateral diffuse or focal infiltrates, pleural effusions or hilar adenopathy.
- **Meningitis** "the most common presentation": There is headache, fever, nausea, personality changes, ... etc.
- **Mucocutaneous lesions** "10-15% of cases", but are pathognomonic usually accompany disseminated disease, in the form of erythema nodosum-like lesions, acneiform papules or pustules, or warty crusted plaques mainly around the nose and mouth. Ulceration may occur leading to BCC-like ulcers.

Diagnosis

- **Direct microscopy of India ink mounts:** Large encapsulated yeast (5-15 μ m).
- **Culture** of sputum, CSF or tissue on malt-extract agar or Sabouraud's agar. The organism is characterized by ability to grow at 30°C – 37°C, absence of pseudohyphae, urease production and ability to assimilate creatinine.
- **Histopathology:** The encapsulated budding cells are seen mixed with a network of connective tissue with minimal inflammatory reaction. Occasionally a granulomatous reaction may be seen without caseation, consisting of necrotic organisms rather than necrotic reactive tissue cells.
- **Serological tests (of CSF):** The cryptococcal latex agglutination test "LCAT" is highly specific and sensitive. It is very useful in screening.

Treatment

- **In the non-AIDS patients:** Amphotericin B IV (0.3 mg/kg/day) + Flucytosine (150 mg/kg/day).

- **In AIDS patients:** Fluconazole is a promising agent mainly in cryptococcal meningitis. Fluconazole or itraconazole may be used as maintenance to prevent recurrences.

Mucormycosis “Zygomycosis”

It is a severe, fulminating fungal infection affecting lungs, CNS, paranasal sinuses, GIT, skin and other parts of body. It is caused by species of *Rhizomucor*, *Absidia* and *Rhizopus*. It commonly affects the severely immunocompromised patients, e.g. leukemia, diabetes, renal failure, ... etc. Infection is acquired usually by inhalation of air-borne spores that settle in the paranasal sinuses or lungs.

Cutaneous mucormycosis is usually a manifestation of disseminated disease and appears as painful erythematous eruptions with varying degrees of necrosis. Invasion of blood vessel walls, with subsequent thrombus formation and black necrotic debris is the main pathologic event of the disease. Direct inoculation of the organism into the skin may occur rarely with contaminated bandages and dressings.

Subcutaneous zygomycosis (subcutaneous phycomycosis): It is caused by ***Basidiobolus haptosporus***. There is a slowly spreading painless subcutaneous swelling of limbs or limb-girdle areas.

Diagnosis is usually made by biopsy of infected tissue which reveals broad and non-septate hyphae extending into blood vessels.

Therapy: IV Amphotericin.

Aspergillosis

It is a fungal disease caused by ***Aspergillus fumigatus*** and ***A. flavus*** and affects mainly lungs of immunocompromised patients and with hematogenous spread, cutaneous, naso-orbital cerebral or disseminated disease can occur.

Fusarium infection*

Etiology: *Fusarium* species. They are molds which are prevalent in the soil and air.

Clinically

- **Localized cutaneous infections:** e.g. onychomycosis and infections of surgical and burn wounds.
- **Disseminated infections:** In patients with severe neutropenia, e.g. acute leukemia or patients undergoing BM transplantation. In about 70% of patients there are skin lesions of multiple red or gray macules, papules (may be with central necrosis), pustules and subcutaneous nodules. Infections fail to respond to antifungal therapy unless there is resolution of the patient's neutropenia.

* J Am Acad Dermatol, 2002; 47.

Culture on sabouraud's glucose-peptone agar of fungi causing deep mycoses

	Antibiotic supplement		Incubation temp.		Incubation time (days)
	Chloramphenicol	Cycloheximide	Room	37°C	
• Dimorphic fungi	+	+	+	+	Variable
• Subcutaneous					
◦ Sporotrichosis					7
◦ Chromomycosis	+	+	+	-	4-10
◦ Mycetoma					
◦ Fungi	+	-	+	+	5-10
◦ Actinomycetes	-	+	+	+	2-3
• Opportunistic					
◦ Cryptococcosis					3-10
◦ Mucormycosis	+	-	-	+	1-3
• Aspergillosis					3-5

- Inflammatory lesions:

1. T. Corporis
2. Candidiasis
3. Seb. Dermatitis
4. Darier Disease
5. Hailey-Hailey Dis -
6. Inverse psoriasis
7. Intertrigo.

- Serpiginous lesion:

1. T. Corporis
2. Contact Dermatitis
3. 2ry Syphilis
4. Granuloma annulare
5. Urticaria
6. Cut. larva - migrans
7. parakeratosis
8. Ichthyosis hystrix
9. parapsoriasis

- Drug of choice:

1. T. Capitis = griseofulvin
2. T. Corporis = Allylamine
3. T. Cruris = Allylamine
4. PVC: Itraconazole - Fluconazole
5. VVC = Fluconazole
6. T. pedis = Itraconazole

- Cicatricial Alopecia

* Infections:

- Fungal: Kerion - Favus
- Mycobact: LV - leprosy
- Viral = HZ
- Protozoa = leishmaniasis

* Congenital: - - -

* Tumors: - - -

* Traumatic = - - -

- Diseases Healed By Scarring:

1. Favus
2. Kerion
3. DLE
4. Ecthyma
5. EB
6. LV
7. PCT

- Hairy scalp pustules Crusts, exudation:

1. Kerion
2. Cont. Dermatitis
3. Acne Keloid
4. pediculosis

- Itching is pathognomic in

1. T. Cruris
2. Pung. Nodularis
3. Hypertrophic LP
4. DH
5. Scabies
6. Mastocytosis
7. Urt. Carica

- Nail colors:

- Yellow → Onychomycosis - lymphedema.
- Orange-Brown → Hemochromatosis - Addison Disease - Hypothyroidism
- Blue: Wilson's Disease. Cyanosis
- Black: Hge. melanoma

- Diseases Related to End Stage Renal Disease:

1. Onychomycosis -
2. T. pedis
3. Xerosis

- Mouth plaques:

1. Candidiasis
2. leukoplakia
3. Hairy leukoplakia
4. lichen planus

- Asteroid Bodies:

- 1 - Sporotrichosis
- 2 - T.B
- 3 - Leprosy
- 4 - Sarcoidosis

- Cigarette paper Scales:

- 1 - PVC
- 2 - P. Resea -

- Mouth Ulcers:

- 1 - Histoplasmosis
- 2 - Carcinoma
- 3 - Behcet Disease
- 4 - Aphthous Ulcers

- Diseases Caused By Cats:

- 1 - Fungal → Dermatophytes
- 2 - Mycobact → T.B
- 3 - Bacterial → Cat scratch Disease - Cellulitis
- 4 - Parasitic → Scabies
Leishmaniasis

- Scales:

- 1 - PVC → Cigarette Paper
- 2 - Psoriasis → laminated silvery white adherent
- 3 - P. resae → collarette
- 4 - DLE → adherent

- Skin Diseases of Breast - Nipple:

- 1 - Candidiasis
- 2 - Acanthosis Nigricans
- 3 - Darier Disease
- 4 - Leiomyomas
- 5 - Breast Cancer
- 6 - Lupus panniculitis
- 7 - Lupus Mastitis

- Skin Diseases of groin:

- 1 - Candidiasis
- 2 - Acanthosis Nigricans
- 3 - Mycosis fungoides
- 4 - Intertrigo
- 5 - Erythrasma
- 6 - Contact Dermatitis
- 7 - Hailey-Hailey Disease

- Napkin Rash:

- 1 - Candidiasis
- 2 - Seb. Dermatitis
- 3 - Psoriasis
- 4 - Contact Dermatitis
- 5 - Miliaria
- 6 - Syphilis

- Lesions

- Koilonychia

- 1 - Candidiasis
- 2 - PRP
- 3 - Reiter's disease
- 4 - Geographic Tongue
- 5 - Keratoderma blennorrhagica

- Axilla lesions:

- 1 - P. Versicolor
- 2 - Acanth. Nigricans
- 3 - Fox - Fordyce Dis
- 4 - Hidradenitis Suppurata
- 5 - Pemphigus
- 6 - Plane Xanthoma

- Hypopigmented Macule Trunk:

- 1 - T. versicolor
- 2 - Morphea
- 3 - Vitiligo
- 4 - Lichen sclerosus et atrophicus
- 5 - Syphilis
- 6 - Scarring DLE
- 7 - Tuberculoid leprosy

Epidermodysplasia verruciformis

- Rare, familial skin disease, AR, begins in childhood
- HPV 5 & 8
- Long standing, wide-spread, flat, wart-like lesion on arms, legs, face & back of hands
- & Macular erythematous PV-like lesion on face, neck, trunk & arm
- May be confluent
- Malignant transformation 50%

PVC

- Common superficial fungal infection
- yeast *Malassezia furfur*
- Sharply demarcated macules covered by branny scales
- Color varies from light brown to pink to hypopigmented white
- Large confluent areas & oval patches
- Affecting seborrheic distribution, upper trunk, neck, upper arm
- Axilla & groin → inverse PVC
- Moderate itching may be present

tr:

- 1- Observation for development of carcinoma & premalignant lesions
- 2- Sunscreen & avoid excessive sun exposure
- 3- Oral retinoids
- 4- Topical imiquimod
- 5- Surgical, electrosurgical, cryotherapy for premalignant lesion
- 6- Surgery for SCC

A) Topical:

- 1- Selenium sulfide
 - 2- Zinc pyrithione
 - 3- Imidazoles
 - 4- Allylamines
- * Hypopigmented lesions: PUVA, steroids

B) Systemic (oral):

- 1- Ketoconazole: 1X1X5-10 d
Or single dose: 400 mg
1X1X3d /month for 6 months to prevent relapse
- 2- Itraconazole: 2X1X5-7 d
- 3- Fluconazole: single dose 300mg
Repeat after 2 weeks
300/month for 6 months to prevent relapse

Tinea imbricata

- Fungal infection caused by *T.concentricum*
- Concentric erythematous scaly rings
- Intense pruritus
- Anti-fungal ttt

Erythema gyratum repense

- One of the figurate erythema
- Associated with carcinoma of lung or breast (Paraneoplastic syndrome)
- Generalized eruption of parallel erythematous bands with annular & serpiginous arrangement with peripheral scaling (Wood-grain appearance)
- Intense pruritus
- Complete resolution after removal of carcinoma

Q Fungal Infections:

- 1- Give account on dermatophytide.
- 2- Infection with yeast.
- 3- Discuss tinea capitis
- 4- Diagnosis of tinea capitis
- 5- Clinical picture & ttt of kerion.
- 6- Discuss TVC
- 7- Mention 4 skin diseases caused by malassezia species.
- 8- Tinea nigra.
- 9- Management of a case of tinea unguium.
- 10- Tinea pedis: predisposing factors, clinical presentation, DD, management.
- 11- Sporotrichosis.
- 12- Compare: black piedra & white piedra
- 13- Compare: white superficial onychomycosis versus disto-lateral onychomycosis.
- 14- Lab diagnosis of superficial fungal infection.
- 15- KOH test findings in : dermatophytes, candida albicans, malassezia furfur.
- 16- How to investigate: mucocutaneous candidiasis, pityriasis versicolor.
- 17- Treatment of superficial fungal infection in children.
- 18- Treatment of ringworm infection.
- 19- Management of pityriasis versicolor.
- 20- Systemic antifungal ttt.
- 21- Griseofulvin (mechanism of action, indications, limitations of use, side effects).
- 22- Systemic first line therapy of choice in tinea capitis, kerion, herpes zoster.

23- Onychomycosis can affect nail plate as well as nail bed: what are different pathogen in such case, different diagnostic methods, different lines of treatments?